REMARKS

Reconsideration of the present application is respectfully requested in view of the Amendment submitted herewith and the following remarks. Claims 19-24 and 26-32 were pending in the Application. To point out more clearly and to claim distinctly certain embodiments of Applicants' invention, claims 19, 22, and 30-32 have been cancelled, claims 20, 21, 23, 24, and 26-29 have been amended, and new claims 33 and 34 have been added. Amendments to the specification have been made solely to correct typographical errors referring to Table numbers in the Examples. Accordingly, upon entry of this Amendment, claims 20, 21, 23, 24, 26-29, and 33-34 are currently under examination. The Amendment submitted herewith is not to be construed as acquiescence to the stated grounds for rejection and is made without prejudice to prosecution of any subject matter modified or removed by this Amendment in a related divisional, continuation, or continuation-in-part application. No new subject matter has been added. Support for the amended and new claims may be found throughout the specification, for example, at page 7, lines 4-15; page 11, lines 28-30; page 12, lines 18-20; page 13, lines 3-7; page 13, line 21 through page 14, line 22; page 14, line 23 through page 15, line 5; page 21, lines 4-30; page 22, lines 1-5; page 24, lines 4-5; page 37, lines 11-17; and page 39, line 23 through page 40, line 6.

Applicants wish to make known to the Examiner that a U.S. divisional application (Application No. 09/938,406) is currently co-pending with the present application.

Information Disclosure Statements

Applicants thank the Examiner for considering the information provided in the Form 1449 that is attached to the Office Action dated August 30, 2005.

Applicants submit herewith a Third Supplemental Information Disclosure Statement and Form 1449. Applicants respectfully request that the Examiner consider these documents and make the cited documents of record in this application. Applicants also request that the Examiner consider the documents submitted with the Information Disclosure Statement submitted to the U.S. Patent and Trademark Office on August 12, 2005, and make the cited documents of record in this application.

Rejections Under 35 U.S.C. § 112, Second Paragraph

In the Office Action dated August 30, 2005, the Examiner has rejected claims 19-24, 26-29 and 31 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. The Examiner alleges that the "claims appear to be directed toward the generation of a mucosal immune response but do not specify any particular route of administration." With respect to "claim 26," [*sic*, claim 27?] the Examiner alleges that the term, "bonding," is vague and does not indicate what type of chemical reaction is encompassed by the term.

Applicants respectfully traverse these rejections and submit that the amended claims submitted herewith particularly point out and distinctly claim the subject matter that Applicants regard as their invention. New claim 33 is directed, in pertinent part, to a process for inducing a neutralizing antibody response in a subject against HIV comprising administering a vaccine composition directly to mucous membranes (*see, e.g.,* specification at page 15, lines 3-6). In certain embodiments, the vaccine composition is administered by an intranasal or respiratory route (*see, e.g.,* specification at page 15, lines 3-6; originally filed claims). Therefore, the present claims clearly and distinctly define that the vaccine composition is administered to a subject in a manner that will elicit a mucosal response.

With respect to claim 27, in a specific embodiment, the process comprises administering a vaccine composition that further comprises an exogenous hydrophobic anchor (*i.e.,* a hydrophobic material (*see, e.g.,* specification, page 11, lines 28-30)), wherein the vaccine composition is formed by adding the hydrophobic anchor (*e.g.,* a C8-C18 fatty acyl group or lauroyl, or a peptide having the amino acid sequence set forth in either SEQ ID NO:2 or SEQ ID NO:3) (*see, e.g.,* specification, at page 11, line 28 through page 14, line 22) to the C-terminal truncated gp160 protein to form an anchored C-terminal truncated gp160 protein. As described in the specification, an exogenous hydrophobic anchor may be added synthetically or recombinantly to either terminus of an antigen, such as a C-terminal truncated gp160 protein (*see, e.g.,* page 11, line 28 through page 12, line 17; page 13, line 16 through page 14, line 2). An exogenous hydrophobic anchor that is a fatty acid may be added to either the amino terminal end or carboxyl end of an antigen (*see, e.g.,* page 12, lines 6-17). The specification also describes that an exogenous hydrophobic anchor that is a peptide may be added synthetically or

recombinantly to either the amino terminus or carboxy terminus of an antigen (*see, e.g.*, page 13, line 16 through page 14, line 14). Accordingly, when read in light of the specification, the claims clearly and distinctly define certain embodiments of Applicants' invention.

Applicants therefore respectfully submit that the present claims meet the requirements for definiteness under 35 U.S.C. § 112, second paragraph, and request that these rejections be withdrawn.

Rejection Under 35 U.S.C. § 102

The Examiner has rejected claims 19 and 30-32 under 35 U.S.C. § 102(e), for allegedly being anticipated by Lowell (U.S. Patent No. 5,726,292; 1998). Applicants submit that in view of the Amendment submitted herewith, which includes cancellation of claims 19 and 30-32 without acquiescence or prejudice, this rejection has been rendered moot.

Rejections Under 35 U.S.C. § 103

The Examiner has rejected claims 22-24, 26, and 29 under 35 U.S.C. § 103(a) for allegedly being obvious over Lowell (1998). The Examiner asserts that Lowell teaches that high molecular weight proteins with endogenous hydrophobic sequences combined with proteosome formulations and administered intranasally are capable of inducing a neutralizing mucosal antibody response. The Examiner acknowledges that Lowell does not teach generation of a mucosal neutralizing antibody response to "a modified gp160." The Examiner also rejects claims 20, 21, and 27-29 under 35 U.S.C. § 103(a) for allegedly being obvious over Lowell. The Examiner asserts that Lowell teaches that proteins with an endogenous sequence can be conjugated to an exogenous hydrophobic sequence and that the polypeptide/hydrophobic foot/proteosome composition can induce a neutralizing mucosal immune response.

Applicants respectfully traverse these rejections and submit that the presently amended claims are nonobvious. Lowell does not teach or suggest each feature of the present claims; nor does Lowell provide any motivation, teaching, or suggestion that a person having ordinary skill in the art would reasonably expect to achieve successfully Applicants' claimed process.

The present claims are directed to a process for inducing a neutralizing antibody response in a subject against HIV, comprising administering a vaccine composition directly to mucous membranes, wherein the vaccine composition comprises (a) an antigen that comprises a C-terminal truncated gp160 protein, wherein the C-terminal truncated gp160 protein includes the endogenous hydrophobic amino acid sequence set forth at positions 523-551 of SEQ ID NO:1; (b) proteosomes, wherein the proteosomes are complexed or coupled with the antigen; and (c) bioadhesive nanoemulsions, wherein the composition elicits neutralizing antibodies to HIV in a subject upon administration of the composition to the subject, and wherein the neutralizing antibodies are present in one or more of vaginal secretions, intestinal secretions, lung secretions, and feces; and to related processes. In other certain embodiments, the C-terminal truncated gp160 protein is a C-terminal truncated gp160 oligomer. In another certain embodiment, the amino acid sequence of the C-terminal truncated gp160 protein consists essentially of the amino acid sequence set forth at residues 33-681 of SEQ ID NO:1. As noted above, the Examiner agrees that Lowell does not teach or suggest "a modified gp160." Lowell specifically does not teach or suggest an antigen that comprises a C-terminal truncated gp160 protein, as recited, nor does Lowell teach or suggest that the amino acid sequence of such a C-terminal truncated gp160 may consist essentially of the sequence set forth at residues 33-681 of SEQ ID NO:1 (*see* claim 24).

Moreover, given the understanding of gp160 in the art, a person having ordinary skill in the art would not reasonably expect to achieve a process for inducing a neutralizing antibody response against HIV by administering a vaccine composition comprising a C-terminal truncated gp160 protein complexed with proteosomes. As understood in the art, the HIV envelope gene encodes the glycoprotein gp160 that is further processed to yield two structural protein portions, gp120 and gp41. The latter portion, gp41, is located at the C-terminal end of gp160 and is the transmembrane portion (*see, e.g.,* specification, page 4, lines 11-18 and references cited therein; Desai et al., *Proc. Natl. Acad. Sci. USA* 83:8380-84 (1986), at page 8383 (a copy of which is attached with the Third Supplemental Information Disclosure Statement submitted herewith)). The transmembrane gp41 moiety of gp160 comprises a membrane-spanning hydrophobic domain, and it also contains amphipathic regions believed to bind to the

plasma membrane (*see, e.g.*, specification, page 6, lines 13-25; Yang et al., *Proc. Natl. Acad. Sci. USA* 92:9871-9875 (1995) (a copy of which is attached with the Third Supplemental Information Disclosure Statement submitted herewith)). Therefore, a person having ordinary skill in the art would reasonably expect that a carboxy terminal truncation of gp160 in the transmembrane gp41 portion would remove one or more hydrophobic portions of transmembrane gp41 (*e.g.*, about 3 to about 50 endogenous non-polar or uncharged amino acid residues) and concomitantly expect that such a C-terminal truncated gp160 protein would be unable to form a complex with proteosomes. In the absence of the disclosure of the subject application, an ordinarily skilled person, therefore, would not reasonably expect to achieve a process for inducing a neutralizing antibody response in a subject against HIV comprising administering a vaccine composition directly to mucous membranes, wherein the composition has the recited features.

Applicants respectfully submit that a *prima facie* case of obviousness has not been established and that the claimed subject matter is nonobvious as required under 35 U.S.C. § 103. Applicants therefore respectfully request that the rejection of the claims be withdrawn.

Applicants respectfully submit that pending claims 20, 21, 23, 24, 26-29, and 33-34 in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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